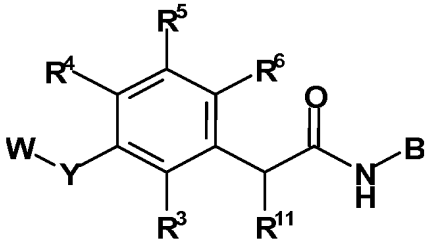
This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Original) A compound of Formula ***I***:



or a solvate, hydrate or pharmaceutically acceptable salt thereof; wherein:

W is R^1 or $R^1S(O_2)$;

R^1 is

R^2,

$R^2(CH_2)_tC(R^{12})_2$, where t is 0-3, and each R^{12} can be the same or different,

$(R^2)(OR^{12})CH(CH_2)_p$, where p is 1-4,

$(R^2)_2(OR^{12})C(CH_2)_p$, where p is 1-4,

$R^2C(R^{12})_2(CH_2)_t$, wherein t is 0-3, and each R^{12} can be the same or different, wherein $(R^{12})_2$ can also form a ring with C represented by C_{3-9} cycloalkyl,

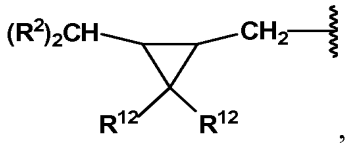
$R^2CF_2C(R^{12})_2(CH_2)_q$, wherein q is 0-2, and each R^{12} can be the same or different, wherein $(R^{12})_2$ can also form a ring with C represented by C_{3-9} cycloalkyl,

$R^2CH_2C(R^{12})_2(CH_2)_q$, wherein q is 0-2, and each R^{12} can be the same or different, wherein $(R^{12})_2$ can also form a ring with C represented by C_{3-9} cycloalkyl,

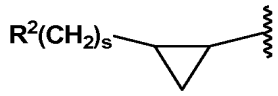
$(R^2)_2CH(CH_2)_r$, where r is 0-4 and each R^2 can be the same or different, and wherein $(R^2)_2$ can also form a ring with CH represented by C_{3-9} cycloalkyl, C_{7-12} bicylic alkyl, C_{10-16} tricylic alkyl, or a 5- to 7-membered mono- or bicyclic heterocyclic ring which can be saturated or unsaturated, and which contains from one to three heteroatoms selected from the group consisting of N, O and S,

$R^2O(CH_2)_p$, wherein p is 2-4,

$(R^2)_2CF(CH_2)_r$, wherein r is 0-4 and each R^2 can be the same or different, wherein $(R^2)_2$ can also form a ring with C represented by C_{3-9} cycloalkyl, C_{7-12} bicyclic alkyl, C_{10-16} tricyclic alkyl, or a 5- to 7-membered mono- or bicyclic heterocyclic ring which can be saturated or unsaturated, and which contains from one to three heteroatoms selected from the group consisting of N, O and S,



,



where s is 0 or 1, or

$R^2CF_2C(R^{12})_2$;

R^2 is

phenyl, naphthyl, or biphenyl, each of which is unsubstituted or substituted with one or more of C_{1-4} alkyl, C_{1-4} alkoxy, halogen, hydroxy, CF_3, OCF_3, COOH, CO_2R^{21}, $CONH_2$, $CONR^{22}R^{23}$, SO_2 alkyl, SO_2NH_2, or $SO_2NR^{22}R^{23}$,

a 5- to 7-membered mono- or a 9- to 10-membered bicyclic heterocyclic or heteroaryl ring, which can be saturated or unsaturated, wherein the heterocyclic or heteroaryl ring contains from one to four heteroatoms selected from the group consisting of N, O and S, wherein the nitrogen and sulfur heteroatoms are optionally oxidized, and wherein the heterocyclic or heteroaryl ring is unsubstituted or substituted with with one or more of C_{1-4} alkyl, C_{1-4} alkoxy, halogen, hydroxy, CF_3, OCF_3, COOH, CO_2R^{21}, $CONH_2$, $CONR^{22}R^{23}$, SO_2 alkyl, SO_2NH_2, or $SO_2NR^{22}R^{23}$,

C_{3-9} cycloalkyl, which is unsubstituted or substituted with one or more of C_{1-4} alkyl, C_{1-4} alkoxy, halogen, hydroxy, CF_3, OCF_3, COOH, CO_2R^{21}, $CONH_2$, $CONR^{22}R^{23}$, SO_2alkyl, SO_2NH_2, or $SO_2NR^{22}R^{23}$, or

C_{7-12} bicyclic alkyl, which is unsubstituted or substituted with one or more of C_{1-4} alkyl, C_{1-4} alkoxy, halogen, hydroxy, CF_3, OCF_3, COOH, CO_2R^{21}, $CONH_2$, $CONR^{22}R^{23}$, SO_2alkyl, SO_2NH_2, or $SO_2NR^{22}R^{23}$;

Y is -NH- or O;

R^3 is hydrogen,halogen or OH;

R^4 and R^5 are independently hydrogen, halogen, alkyl, alkenyl, alkynyl, hydroxy, alkoxy, haloalkyl, haloalkoxy, hydroxyalkyl, cyano, nitro, $-CO_2R^x$, $-CH_2OR^x$ or $-OR^x$, where R^x, in each instance, is independently one of hydrogen or C_{1-6} alkyl;

R^6 is cyano or acetylenyl;

R^{11} is hydrogen, halogen or alkyl;

R^{12} is

hydrogen or halogen,

C_{1-6} alkyl, unsubstituted or substituted with one or more of hydroxy,

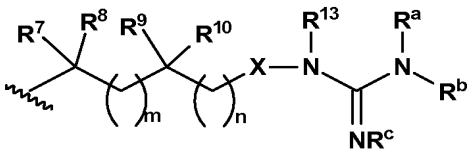
COOH, amino, or halogen,

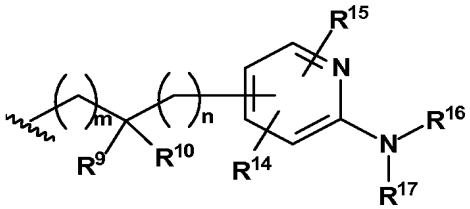
CF_3;

R^{21} is C_{1-8} alkyl, C_{1-8} cycloalkyl, C_{1-8} alkyl ether, or C_{1-8} cycloalkyl ether;

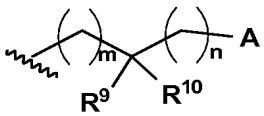
R^{22} and R^{23} are, independently, hydrogen, C_{1-8} alkyl, C_{1-8} cycloalkyl, C_{1-8} alkyl ether, or C_{1-8} cycloalkyl ether or taken together with the nitrogen atom to which they are attached, R_{22} and R_{23} form a 3 to 9 member saturated ring, optionally having from 0 to 2 additional heteroatoms selected from nitrogen or oxygen;

B is selected from the group consisting of:





and



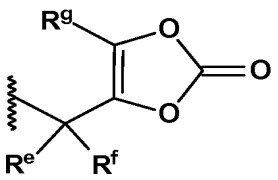
wherein

R^7, R^8, R^9, and R^{10} are independently hydrogen or alkyl;

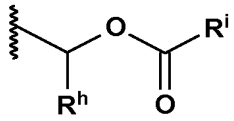
X is -O-, -NR^{18}-, or -CH=N- (where N is bonded to NR^{13}) where R^{18} is hydrogen or alkyl, wherein said alkyl is optionally substituted with amino, monoalkylamino, dialkylamino, alkoxy, hydroxy, carboxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, acylamino, cyano or trifluoromethyl;

R^a, R^b and R^c are independently hydrogen, alkyl, hydroxy, alkoxy, alkoxycarbonyloxy, cyano or $–CO_2R^w$,

where R^w is C_{1-12} alkyl, C_{3-9} cycloalkyl, C_{6-14} aryl, C_{6-14}ar(C_{1-12}) alkyl,



or



where R^e and R^f are independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl or C_{6-14} aryl, R^g is hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl or C_{6-14} aryl, R^h is hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl or C_{6-14} aryl, and R^i is C_{6-14}ar(C_{1-12})alkyl or C_{1-12} alkyl;

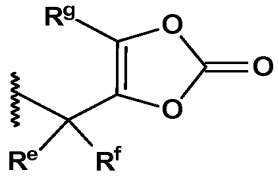
n is from zero to 2;

m is from zero to 2;

R^{13} is hydrogen or alkyl;

R^{14} and R^{15} are independently hydrogen, alkyl, cycloalkyl, halogen or alkoxy;

R^{16} and R^{17} are independently hydrogen, alkyl, hydroxy, alkoxy, cyano or $-CO_2R^j$, where R^j is C_{1-12} alkyl, C_{3-9} cycloalkyl, C_{6-14} aryl, C_{6-14}ar(C_{1-12})alkyl, halo(C_{1-12})alkyl or



where R^e, R^f and R^g are independently hydrogen or C_{1-12} alkyl; and

A is a 9- to 10- membered bicyclic heterocyclic or heteroaryl ring which can be saturated or unsaturated,

wherein the heterocyclic or heteroaryl ring contains from three to five heteroatoms selected from the group consisting of N, O and S, and is optionally substituted with one or more of halogen, hydroxy, alkyl, alkoxy, or $-NR^{19}R^{20}$, where R^{19} and R^{20} are independently hydrogen or C_{1-4} alkyl,

or wherein the heterocyclic or heteroaryl ring contains from one to two heteroatoms selected from N, and is monosubstituted with $-NR^{19}R^{20}$, where R^{19} and R^{20} are independently hydrogen or C_{1-4} alkyl,

or wherein the heterocyclic or heteroaryl ring contains from one to two heteroatoms selected from the group consisting of N, O, S, one of which must be either O or S, and is optionally substituted with one or more of halogen, hydroxy, alkyl, alkoxy, or $-NR^{19}R^{20}$, where R^{19} and R^{20} are independently hydrogen or C_{1-4} alkyl.

2. (Original) A compound of claim 1, wherein R^2 is

phenyl, naphthyl, or biphenyl, each of which is unsubstituted or substituted with one or more of C_{1-4} alkyl, C_{1-4} alkoxy, halogen, hydroxy, CF_3, OCF_3, COOH, $CONH_2$, or SO_2NH_2,

a 5- to 7-membered mono- or a 9- to 10-membered bicyclic heterocyclic or heteroaryl ring, which can be saturated or unsaturated, wherein the heterocyclic or heteroaryl ring contains from one to four heteroatoms selected from the group consisting of N, O and S, and is optionally substituted with halogen, hydroxy, or alkyl,

C_{3-9} cycloalkyl which can be saturated or unsaturated, or

C_{7-12} bicyclic alkyl which can be saturated or unsaturated.

3. (Original) A compound of claim 1, wherein R^3 is hydrogen or halogen and R^{11} is hydrogen or alkyl.

4. (Original) A compound of claim 1, wherein

R^3 is halogen;

R^4 and R^5 are independently hydrogen, halogen, or C_{1-6} alkyl;

R^{11} is hydrogen or C_{1-6} alkyl;

R^7, R^8, R^9 and R^{10} are independently hydrogen or C_{1-6} alkyl;

R^{18} is hydrogen or C_{1-6} alkyl optionally substituted with amino, mono(C_{1-6})alkylamino, di(C_{1-6})alkylamino, C_{1-8} alkoxy, hydroxy, carboxy, C_{1-8}alkoxycarbonyl, C_{6-14} aryloxycarbonyl, C_{6-14}ar(C_{1-20})alkoxycarbonyl, acylamino, cyano or trifluoromethyl;

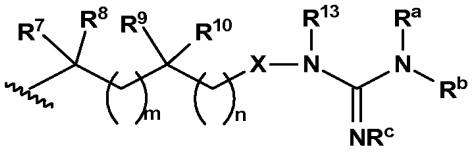
R^a, R^b and R^c are independently hydrogen or C_{1-6} alkyl;

R^{13} is hydrogen or C_{1-6} alkyl;

R^{14} and R^{15} are independently hydrogen or C_{1-6} alkyl; and

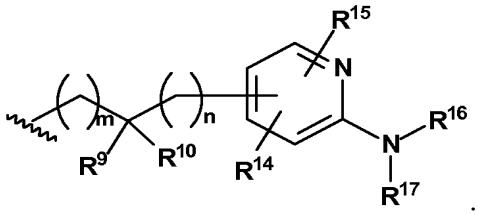
R^{16} and R^{17} are independently hydrogen or C_{1-6} alkyl.

5. (Original) A compound according to claim 1, wherein B is



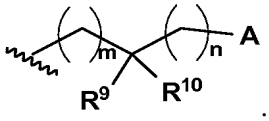
6. (Original) A compound according to claim 5, wherein X is O.

7. (Original) A compound according to claim 1, wherein B is



8. (Original) A compound according to claim 7, wherein R^{16} and R^{17} are hydrogen.

9. (Original) A compound according to claim 1, wherein B is



10. (Original) A compound according to claim 9, wherein A is 3-aminobenzisoxazolyl or benzotetrazolyl.

11. (Original) A compound according to claim 1, wherein:

W is R^1;

R^1 is $R^2CF_2C(R^{12})_2(CH_2)_q$;

R^2 is aryl, pyridyl, or quinolinyl, any of which is optionally substituted with halogen or alkyl;

R^{12} is hydrogen; and

q is zero.

12. (Original) A compound according to claim 1, wherein:

W is R^1;

R^1 is $R^2CF_2C(R^{12})_2(CH_2)_q$;

R^2 is aryl, pyridyl, pyridyl-N-oxide, quinolinyl or quinolinyl-N-oxide, any of which is optionally substituted with halogen, alkyl or SO_2 alkyl;

R^{12} is hydrogen; and

q is zero.

13. (Original) A compound according to claim 1, wherein R^3 is halogen.

14. (Original) A compound according to claim 13, wherein R^3 is chloro or fluoro.

15. (Original) A compound according to claim 14, wherein R^3 is fluoro while R^4 and R^5 are hydrogen.

16. (Original) A compound according to claim 1, wherein R^{11} is hydrogen.

17. (Original) A compound according to claim 1, wherein R^a, R^b, R^c and R^{13} are each hydrogen.

18. (Original) A compound according to claim 1, wherein each of R^7, R^8, R^9 and R^{10} are hydrogen.

19. (Original) A compound according to claim 1, wherein R^6 is cyano.

20. (Original) A compound according to claim 19, wherein R^3 is halogen.

21. (Original) A compound according to claim 20, wherein R^3 is fluoro while R^4 is hydrogen or fluoro and R^5 is hydrogen.

22. (Original) A compound of claim 1, which is one of:

N-[2-(Amidinoaminooxy)ethyl]-2-{3-[(2,2-difluoro-2-(5-methyl

pyridyl)ethyl)amino]-6-cyano-2-fluorophenyl}acetamide;

N-[2-(Amidinoaminooxy)ethyl]-2-{3-[2-(3-chlorophenyl)-2,2-difluoro ethylamino]-6-cyano-2-fluorophenyl}acetamide;

N-(3-Aminobenzo[d]isoxazol-6-ylmethyl) –2-[6-cyano-3-(2,2-difluoro-2-pyridin-2-yl-ethylamino)-2-fluorophenyl]acetamide;

N-[2-(Amidinoaminooxy)ethyl]-2-{3-[(2,2-difluoro-2-(4-methyl pyridyl)ethyl)amino]-6-cyano-2-fluorophenyl}acetamide;

N-[2-(Amidinoaminooxy)ethyl]-2-{3-[(2,2-difluoro-2-(6-methyl pyridyl)ethyl)amino]-6-cyano-2-fluorophenyl}acetamide;

N-[2-(Amidinoaminooxy)ethyl]-2-{3-[(2,2-difluoro-2-(3-methyl pyridyl)ethyl)amino]-6-cyano-2-fluorophenyl}acetamide;

N-[2-(Amidinoaminooxy)ethyl]-2-{3-[(2,2-difluoro-2-(quinolin-8-yl) ethyl)amino]-6-cyano-2-fluorophenyl}acetamide;

N-(6-Amino-2-methyl-pyridin-3-ylmethyl)-2-[6-cyano-3-(2,2-difluoro-2-pyridin-2-yl-ethylamino)-2-fluoro-phenyl]-acetamide;

N-(6-Amino-pyridin-3-ylmethyl)-2-[6-cyano-3-(2,2-difluoro-2-pyridin-2-yl-ethylamino)-2-fluoro-phenyl]-acetamide;

N-[2-(Amidinoaminooxy)ethyl]-2-{3-[(2,2-difluoro-2-pyridyl ethyl)amino]-6-cyano-2-fluorophenyl}acetamide;

N-[2-(Amidinoaminooxy)ethyl]-2-{3-[(2,2-difluoro-2-phenyl ethyl)amino]-6-cyano-2-fluorophenyl}acetamide;

N-[2-(Amidinoaminooxy)ethyl]-2-{3-[(2,2-difluoro-2-(3-fluoro phenyl)ethyl)amino]-6-cyano-2-fluorophenyl}acetamide;

N-[2-(Amidinoaminooxy)ethyl]-2-{3-[(2,2-difluoro-2-(3,4-difluoro phenyl)ethyl)amino]-6-cyano-2-fluorophenyl}acetamide;

N-[2-(Amidinoaminooxy)ethyl]-2-{6-cyano-3-[2,2-difluoro-2-(6-methyl-1-oxy-pyridin-2-yl)-ethylamino]-2-fluoro-phenyl}acetamide;

N-[2-(Amidinoaminooxy)ethyl]-2-{3-[(2,2-difluoro-2-(5-chloro-pyridin-2-yl)ethyl)amino]-6-cyano-2-fluorophenyl}acetamide;

N-[2-(Amidinoaminooxy)ethyl]-2-{3-[(2,2-difluoro-2-(5-chloro-1-oxy-pyridin-1-yl)ethyl)amino]-6-cyano-2-fluorophenyl}acetamide;

N-[2-(Amidinoaminooxy)ethyl]-2-{6-cyano-3-[2,2-difluoro-2-(1-oxy-pyridin-2-yl)-ethylamino]-2-fluoro-phenyl}acetamide;

N-[2-(Amidinoaminooxy)ethyl]-2-{3-[(2,2-difluoro-2-(2-methanesulfonylphenyl)ethyl)amino]-6-cyano-2-fluorophenyl}acetamide;

N-[2-(Amidino-N-methyl-aminooxy)ethyl]-2-{3-[(2,2-difluoro-2-pyridyl-ethyl)amino]-6-cyano-2-fluorophenyl}acetamide;

2-[6-Cyano-3-(2,2-difluoro-2-pyridin-2-yl-ethylamino)-2-fluorophenyl]-N-tetrazolo[1,5-b]pyridazin-6-ylmethyl-acetamide;

or a solvate, hydrate or pharmaceutically acceptable salt thereof.

23. (Original) A pharmaceutical composition, comprising a compound of claim 1 and a pharmaceutically-acceptable carrier.

24. (Original) A pharmaceutical composition, comprising a compound of claim 2 and a pharmaceutically-acceptable carrier.

25. (Original) A pharmaceutical composition, comprising a compound of claim 5 and a pharmaceutically-acceptable carrier.

26. (Original) A pharmaceutical composition, comprising a compound of claim 7 and a pharmaceutically-acceptable carrier.

27. (Original) A pharmaceutical composition, comprising a compound of claim 9 and a pharmaceutically-acceptable carrier.

28. (Original) A pharmaceutical composition, comprising a compound of claim 19 and a pharmaceutically-acceptable carrier.

29. (Original) A pharmaceutical composition, comprising a compound of claim 20 and a pharmaceutically-acceptable carrier.

30. (Original) A pharmaceutical composition, comprising a compound of claim 22 and a pharmaceutically-acceptable carrier.

31. (Original) A pharmaceutical composition according to claim 23, further comprising at least one of an anticoagulant, an antiplatelet agent or a thrombolytic agent.

32. (Original) A pharmaceutical composition according to claim 23, wherein said compound is present in an amount between about 0.1 and about 500 mg.

33. (Original) A method of inhibiting or treating aberrant proteolysis, thrombosis, ischemic, stroke, restenosis or inflammation in a mammal in need thereof, comprising administering to said mammal an effective amount of a compound of claim 1.

34. (Original) A pharmaceutical composition according to claim 24, further comprising at least one of an anticoagulant, an antiplatelet agent or a thrombolytic agent.

35. (Original) A pharmaceutical composition according to claim 24, wherein said compound is present in an amount between about 0.1 and about 500 mg.

36. (Original) A method of inhibiting or treating aberrant proteolysis, thrombosis, ischemic, stroke, restenosis or inflammation in a mammal in need thereof, comprising administering to said mammal an effective amount of a compound of claim 2.

37. (Original) A method of inhibiting or treating aberrant proteolysis, thrombosis, ischemic, stroke, restenosis or inflammation in a mammal in need thereof, comprising administering to said mammal an effective amount of a compound of claim 5.

38. (Original) A method of inhibiting or treating aberrant proteolysis, thrombosis, ischemic, stroke, restenosis or inflammation in a mammal in need thereof, comprising administering to said mammal an effective amount of a compound of claim 7.

39. (Original) A method of inhibiting or treating aberrant proteolysis, thrombosis, ischemic, stroke, restenosis or inflammation in a mammal in need thereof, comprising administering to said mammal an effective amount of a compound of claim 9.

40. (Original) A method of inhibiting or treating aberrant proteolysis, thrombosis, ischemic, stroke, restenosis or inflammation in a mammal in need thereof, comprising administering to said mammal an effective amount of a compound of claim 19.

41. (Original) A method of inhibiting or treating aberrant proteolysis, thrombosis, ischemic, stroke, restenosis or inflammation in a mammal in need thereof, comprising administering to said mammal an effective amount of a compound of claim 20.

42. (Original) A method of inhibiting or treating aberrant proteolysis, thrombosis, ischemic, stroke, restenosis or inflammation in a mammal in need thereof, comprising administering to said mammal an effective amount of a compound of claim 22.

43. (Original) A method for the treatment or prophylaxis of states characterized by abnormal venous or arterial thrombosis involving either thrombin production or action in a mammal in need thereof, comprising administering to said mammal a composition of claim 23.

44. (Original) A method for the treatment or prophylaxis of states characterized by abnormal venous or arterial thrombosis involving either thrombin production or action in a mammal in need thereof, comprising administering to said mammal a composition of claim 24.

45. (Original) A medical device for use in blood collection, blood storage or blood circulation, comprising a compound of claim 1 embedded in or physically attached to said medical device.

46. (Original) A medical device for use in blood collection, blood storage or blood circulation, comprising a compound of claim 2 embedded in or physically attached to said medical device

47. (Original) A medical device for use in blood collection, blood storage or blood circulation, comprising of claim 5 embedded in or physically attached to said medical device.

48. (Original) A medical device for use in blood collection, blood storage or blood circulation, comprising of claim 7 embedded in or physically attached to said medical device.

49. (Original) A medical device for use in blood collection, blood storage or blood circulation, comprising of claim 9 embedded in or physically attached to said medical device.

50. (Original) A medical device for use in blood collection, blood storage or blood circulation, comprising of claim 19 embedded in or physically attached to said medical device.

51. (Original) A medical device according to claim 45, which is a catheter, stent, blood dialysis machine, blood collection syringe or tube, or a blood line.

52. (Original) A method of inhibiting the action of a proteolytic enzyme, comprising contacting said enzyme with a compound of claim 1.

53. (Original) A method according to claim 52, wherein said enzyme is leukocyte neutrophil elastase, chymotrypsin, trypsin, urokinase, plasminogen activator, pancreatic elastase, cathepsin G, thrombin or factor Xa.

54. (Original) A method of inhibiting the action of a proteolytic enzyme, comprising contacting said enzyme with a compound of claim 2.

55. (Original) A method according to claim 54, wherein said enzyme is leukocyte neutrophil elastase, chymotrypsin, trypsin, urokinase, plasminogen activator, pancreatic elastase, cathepsin G, thrombin or factor Xa.

56. (Original) A method of inhibiting the action of a proteolytic enzyme, comprising contacting said enzyme with a compound of claim 5.

57. (Original) A method according to claim 56, wherein said enzyme is leukocyte neutrophil elastase, chymotrypsin, trypsin, urokinase, plasminogen activator, pancreatic elastase, cathepsin G, thrombin or factor Xa.

58. (Original) A method of inhibiting the action of a proteolytic enzyme, comprising contacting said enzyme with a compound of claim 7.

59. (Original) A method according to claim 58, wherein said enzyme is leukocyte neutrophil elastase, chymotrypsin, trypsin, urokinase, plasminogen activator, pancreatic elastase, cathepsin G, thrombin or factor Xa.

60. (Original) A method of inhibiting the action of a proteolytic enzyme, comprising contacting said enzyme with a compound of claim 19.

61. (Original) A method according to claim 60, wherein said enzyme is leukocyte neutrophil elastase, chymotrypsin, trypsin, urokinase, plasminogen activator, pancreatic elastase, cathepsin G, thrombin or factor Xa

62. (Original) A method of inhibiting the action of a proteolytic enzyme, comprising contacting said enzyme with a compound of claim 22.

63. (Original) A method according to claim 62, wherein said enzyme is leukocyte neutrophil elastase, chymotrypsin, trypsin, urokinase, plasminogen activator, pancreatic elastase, cathepsin G, thrombin or factor Xa

64. (Original) A pharmaceutical composition according to claim 23 adapted for oral administration.

65. (Original) A pharmaceutical composition according to claim 24 adapted for oral administration.

66. (Original) A pharmaceutical composition according to claim 25 adapted for oral administration.

67. (Original) A pharmaceutical composition according to claim 26 adapted for oral administration.

68. (Original) A pharmaceutical composition according to claim 27 adapted for oral administration.

69. (Original) A pharmaceutical composition according to claim 28 adapted for oral administration.

70. (Original) A pharmaceutical composition according to claim 29 adapted for oral administration.

71. (Original) A pharmaceutical composition according claim to 30 adapted for oral administration.